



NOTES LYMPHOMAS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Lymphocytic tumors
- **Nodal lymphomas:** develop in lymph nodes
- **Extranodal lymphomas:** develop in/spread to other organs/tissues
- Neoplastic B cells do not produce antibodies
- Attract non-neoplastic inflammatory cells (e.g. T cells) via chemokines
- Activate fibroblasts to make collagen, eosinophils

TYPES

Hodgkin's lymphomas

- Spread contiguously (to nearby lymph nodes; rarely extranodal)
 - *Prognosis better for Hodgkin's:* contiguous spread allows direct, targeted treatment
- Reed–Sternberg cells

Non-Hodgkin's lymphomas

- Spread non-contiguously
- No Reed–Sternberg cells

CAUSES

- Genetic mutation in lymphocytes → no apoptosis → cell divides → becomes neoplastic cell
- Possible link between viruses (e.g. HIV, EBV), lymphomas

COMPLICATIONS

- Metastasis to spinal cord → spinal cord compression → sensory/motor deficits

- Metastasis to bone marrow → crowds out normal marrow progenitor cells → decreases healthy erythrocytes/leukocytes/platelets

SIGNS & SYMPTOMS

- **B (systemic) symptoms:** fever, night sweats, weight loss, fatigue, loss of appetite, chills

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan, positron emission tomography (PET) scan

- Stage of lymphoma

LAB RESULTS

Lymph node biopsy

- Confirmation, type

TREATMENT

- Depends on extent, stage, category; age, health of individual; coexisting diseases

MEDICATIONS

- Chemotherapy

SURGERY

- Stem cell transplant

OTHER INTERVENTIONS

- Radiation therapy

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HODGKIN'S VS. NON-HODGKIN'S

	HODGKIN'S LYMPHOMA	NON-HODGKIN'S LYMPHOMA
OCCURRENCE	Bimodal: young adulthood; > 55y	Children and adults; risk increases with age
CELLULAR CHARACTERISTICS	B cells, Reed-Sternberg cells	B cells, T cells, natural killer (NK) cells
NODE INVOLVEMENT	Contiguous spread	Non-contiguous spread; extranodal
TYPES	Classic (nodular sclerosis, mixed cellularity, lymphocyte-depleted, lymphocyte-rich) Nodular lymphocyte predominant (has popcorn cells & no Reed-Sternberg cells)	Small lymphocytic, lymphoplasmacytic, extranodal marginal zone (MALT), follicular, mantle cell, diffuse large B-cell, Burkitt, precursor T-lymphoblastic, peripheral T-cell
PRESENTATION	Painless localized lymphadenopathy "B" symptoms	Painless localized lymphadenopathy; "B" symptoms and/or symptoms of extranodal spread
RISK FACTORS	Associated with EBV	Associated acquired or congenital immunodeficiency Endemic Burkitt lymphoma closely associated with EBV

HODGKIN'S LYMPHOMA

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PATHOLOGY & CAUSES

- B-cell tumors; Reed-Sternberg cells: large mononuclear, neoplastic cells; two cells fused, two nuclei (resemble owl eyes)

TYPES

Classical Hodgkin's lymphoma (CHL)

- More common
- Reed-Sternberg cells express CD45/CD20; not CD15/CD30
- Histological subtypes: background inflammatory cells, fibrosis

Histological CHL subtypes

- Nodular sclerosis Hodgkin's lymphoma
 - Most common; esp. in young adults
 - Neoplastic, inflammatory cells surrounded by collagen from fibroblasts forming nodules
 - Lacunar cells (Reed-Sternberg cells with shrunken cytoplasm, nucleus appears as if in middle of lacuna/lake)
 - Good prognosis
- Mixed cellularity
 - Second most common; more common in older adults
 - Prevalent in HIV-positive individuals
 - Mixed inflammatory background

composed of eosinophils, neutrophils, plasma cells, histiocytes surrounding **Reed–Sternberg cells**

- Lymphocyte-rich
 - Reed–Sternberg cells surrounded by lymphocytes
 - **Best prognosis**, caught early
- Lymphocyte-depleted
 - **Rarest**; **median age**: 30–37 years
 - No reactive lymphocytes, abundance of Reed–Sternberg cells
 - Prevalent in **HIV-positive** individuals
 - Worst prognosis, advanced stage diagnosis

Nodular lymphocyte predominant Hodgkin's lymphoma

- More common in individuals who are biologically male
- **Abnormal B cells** express CD20/CD45; not CD15/CD30
- Lymphocyte-predominant cells; no Reed–Sternberg cells
 - Large groups of lymphocytes form nodules around lobulate-nucleated “popcorn” cells (variant of Reed–Sternberg cells)
- Slow-growing, highly curable
- Small risk of transformation to aggressive non-Hodgkin's lymphoma

STAGING

- **Stage 1**: limited to one lymph node group/group of adjacent lymph nodes
- **Stage 2**: $\geq$ two lymph node regions on same side as diaphragm
- **Stage 3**: lymph nodes on both sides (superior, inferior) of diaphragm
- **Stage 4**: lymph nodes superior, inferior to diaphragm; liver/spleen/lungs/bone marrow
- Subdivisions
 - **Category A**: no symptoms
 - **Category B**: B symptoms present
 - **Category E**: organs/tissues beyond lymph system

SIGNS & SYMPTOMS

- Painless cervical lymphadenopathy
 - **Mediastinal lymphadenopathy**: nodular sclerosis subtype
- **Cytokine release**: fever, drenching night sweats, weight loss
 - Rarely present with nodular lymphocyte predominant Hodgkin's lymphoma
- B symptoms
 - **Nodular sclerosis**: about 50%
 - **Mixed cellularity**: common
 - **Lymphocyte-rich**: rare
 - **Lymphocyte-depleted**: common

DIAGNOSIS

DIAGNOSTIC IMAGING

- CT scan, PET scan

LAB RESULTS

- Lymph node biopsy

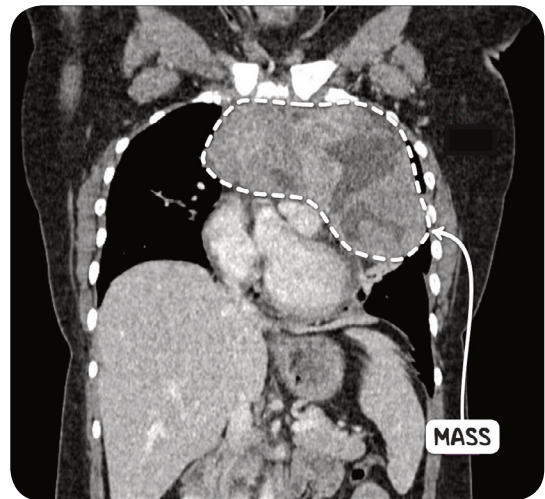


Figure 49.1 A CT scan of the chest in the coronal plane demonstrating a large mediastinal mass. The mass is a focus of Hodgkin's lymphoma.

TREATMENT

MEDICATIONS

Rituximab

- For nodular lymphocyte predominant Hodgkin's lymphoma
- Monoclonal antibody, binds CD20, induces complement-mediated lysis → apoptosis

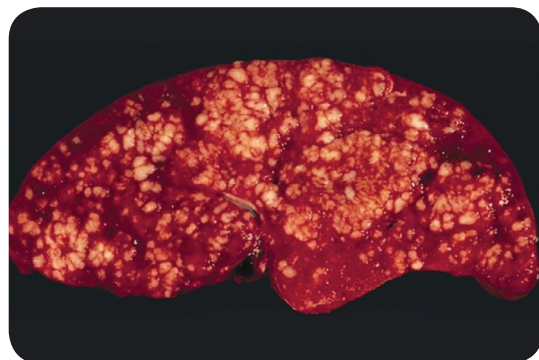


Figure 49.3 The gross pathology of a spleen that has been infiltrated by Hodgkin's lymphoma.

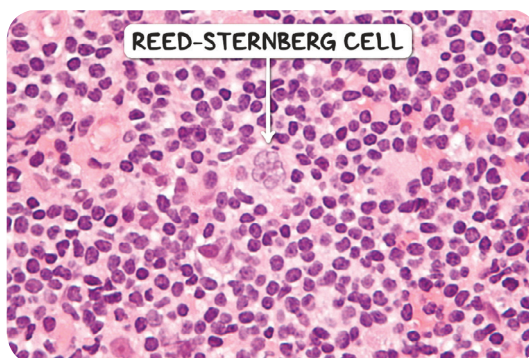


Figure 49.2 The histological appearance of Hodgkin's lymphoma. Reed–Sternberg cells are pathognomonic of this disease.

NON-HODGKIN'S LYMPHOMA

osms.it/non-hodgkin

PATHOLOGY & CAUSES

- B/T cell tumors, no Reed–Sternberg cells

TYPES

B cell lymphomas

- More common
- Neoplastic B cells: CD20 on surface
- Rate of growth: slow/aggressive/highly aggressive

B cell lymphoma subtypes

- Diffuse large B cell lymphoma
 - Aggressive
 - Most common
- Follicular lymphoma

- Slow growing
- Chromosomal translocation: t(14,18) → BCL2 gene placed after Ig heavy chain promoter → overexpression of BCL2 → inhibition of apoptosis → cell proliferation
- BCL2 promotes cell viability, blocks apoptosis
- Burkitt lymphoma
 - Highly aggressive
 - “Starry sky” appearance under microscope
 - Stars: tingible bodies (macrophages) with phagocytosed dead neoplastic cells
 - Sky: dark neoplastic lymphocytes
 - Chromosomal translocation: t(8,14) → Myc gene moved adjacent to IgH

promoter sequence → upregulation of Myc gene → **Myc gene stimulates cell growth**, metabolism → increased cell division

- **Variant in individuals of African descent:** extranodal involvement of **jaw**, associated with **EBV infection**
- **Variant in individuals of non-African descent:** extranodal involvement of **abdomen** (e.g. at ileocecal junction), less frequently associated with EBV infection
- **Mantle cell lymphoma**
 - Aggressive
 - **Chromosomal translocation:** t (11,14) → BCL1 gene moved to Ig promoter → upregulation of BCL1 gene → stimulation of cell growth
- **Marginal zone lymphoma**
 - Indolent
 - Most common type
 - Associated with **mucosa-associated lymphoid tissue** (extranodal) in cases of chronic inflammation of stomach lining (e.g. chronic H. pylori infection)
 - May occur in lymph nodes (nodal marginal zone lymphoma)/spleen (splenic marginal zone lymphoma)
- **Lymphoplasmacytic lymphoma**
 - Indolent
 - Bone marrow, lymph nodes, spleen
 - **Waldenstrom macroglobulinemia:** neoplastic cells produce M proteins (IgM) in high levels → IgM released into

TYPES OF NON-HODGKIN'S LYMPHOMAS

	OCCURRENCE	CHARACTERISTICS
BURKITT (VERY AGGRESSIVE)	Adolescents, young adults	Arises from germinal center B cell; Clinical forms: endemic, sporadic, immunodeficiency-associated; "Starry sky" appearance
DIFFUSE LARGE B CELL (AGGRESSIVE)	Mostly adults (Most common type)	Arises from germinal center or post-germinal center B cell; Diffuse extranodal involvement, often present in GI tract; Variant arises from thymic (medullary) B cells
EXTRANODAL MARGINAL ZONE (MALT) (SLOW GROWTH)	Mostly adults (Risk ↑ with age)	Arises from B cells of the mucosa-associated lymphoid tissue (MALT) Often present in GI tract; Gastric MALT lymphoma linked with H. pylori Forms lymphoepithelial lesions
FOLLICULAR (SLOW GROWTH)	Adults	Arises from germinal center B cells (centrocytes and centroblasts); Painless, relapsing/remitting pattern of lymphadenopathy; Microscopic and gross nodular appearance May transform into more aggressive NHL
LYMPHOPLASMACYTIC	Adults (Risk ↑ with age)	Arises from peripheral B lymphocytes; Manifests from Waldenström macroglobulinemia; Malignant cells resemble plasma cells with large amounts of basophilic cytoplasm; Nucleus contains "spoke wheel -like" chromatin
MANTEL CELL (MODERATELY AGGRESSIVE)	Adults (Risk ↑ with age)	Arises from pre-germinal center B cells of the mantle zone; Results from deregulation of cyclin D1; Diffuse growth pattern; Cells have "notched" nuclei

blood → increases blood viscosity

T cell lymphomas

- Adult T cell lymphoma
 - AKA *leukemia*: abnormal leukocytes in bloodstream
 - Possibly cause: human T-lymphotropic virus (HTLV)
 - HTLV infects T cells → becomes incorporated into T cell DNA → genetic mutation → adult T cell lymphoma
- Mycosis fungoides
 - T cell lymphoma of skin, resembles fungal infection
 - Neoplastic cells: CD4+ helper T cells circulate in blood → Sezary syndrome (erythroderma)

SIGNS & SYMPTOMS

- Painless lymphadenopathy
- B symptoms: release of cytokines
- Extranodal involvement of GI tract: bowel obstruction
- Extranodal involvement of bone marrow: fatigue, easy bruising, recurrent infections
- Extranodal involvement of spinal cord: motor/sensory deficits (esp. legs)

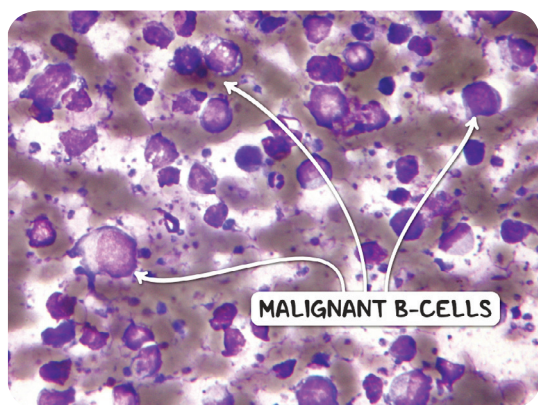


Figure 49.5 A diffuse large B-cell lymphoma in a cytology specimen.

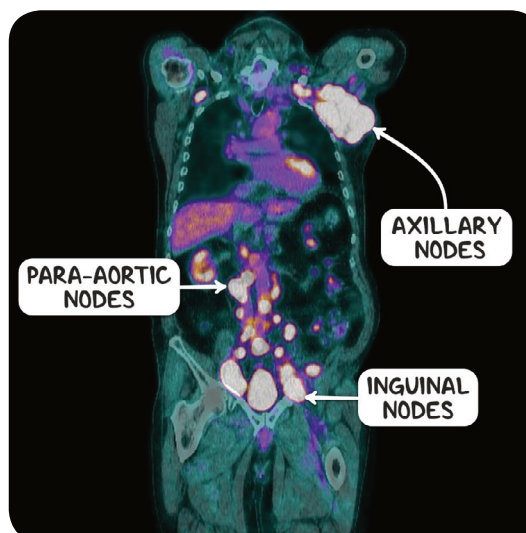


Figure 49.4 A PET scan in the coronal plane demonstrating gross lymphadenopathy in the axillary, para-aortic and inguinal chains. The underlying cause is a Non-Hodgkin lymphoma.

DIAGNOSIS

DIAGNOSTIC IMAGING

- CT scan, PET scan

LAB RESULTS

- Lymph node biopsy

TREATMENT

MEDICATIONS

Rituximab

- CD20-positive B cell non-Hodgkin lymphomas

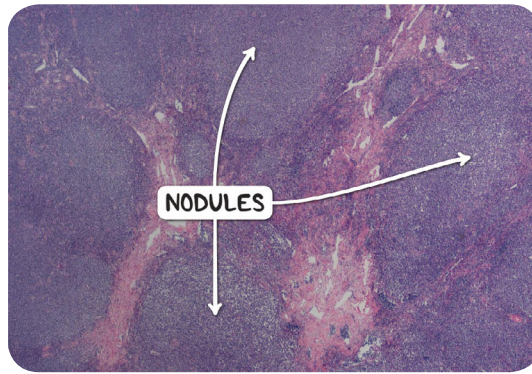


Figure 49.6 The histological appearance of mantle cell lymphoma at low power. This lymph node has been infiltrated by the malignant lymphocytes which have a vaguely nodular architecture.

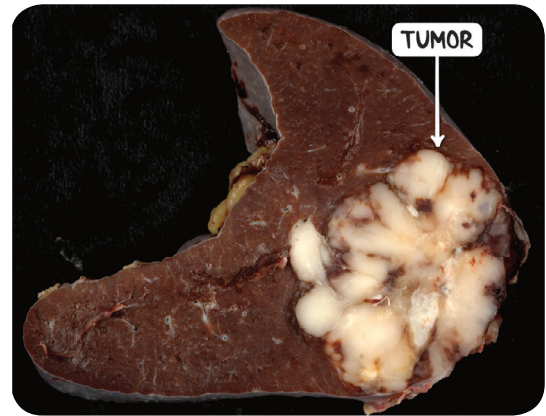


Figure 49.7 A diffuse large B-cell lymphoma in a cytology specimen.